



Health Services Research Unit

Newsletter

Spring 2012

Successful Quinquennial Review

Every five years the Unit undergoes rigorous review by its funder, the Chief Scientist Office of the Scottish Government Health Directorates. The review takes the form of a two-stage process. First, the strategic value of a health services research unit to Scotland (and the extent to which HSRU currently meets this need) is undertaken. This involves the Unit preparing a document outlining the strategic case for the Unit and staff from the Chief Scientist's Office conducting a series of interviews with a range of key external stakeholders. If the strategic case is successful, the second stage involves a formal scientific review (and two-day visit) by a team of independent experts who review the Unit's past work and plans for the future.

2011 marked the latest review of the Unit, with the strategic case presented in

June 2011 and the independent scientific review which took place in November 2011. The Unit's work was highly acclaimed at both stages of the review. In their conclusion, the independent scientific review team commented that *"... the Unit's performance over the past 5 years had been outstanding. Both substantive programmes of work [i.e. Health Care Assessment and Delivery of Care] were world class."* Core funding for the Unit has now been approved for a further five years.

This successful scientific review provides an excellent platform for the Unit to plan for the next five year period with confidence. The broad thrust of the future plans of our two large programmes were endorsed by the review team and helpful recommendations made.

MAPS Trial Publishes Findings

MAPS was a randomised controlled trial, in 34 UK centres, of conservative treatment for urinary incontinence in men after (a) radical prostatectomy or (b) transurethral resection of prostate (TURP). The aim was to determine the effectiveness and cost-effectiveness of active conservative treatment delivered one-to-one by trained therapists, compared with standard management, in regaining urinary continence at 12 months in men with urinary incontinence at six weeks after surgery. Eligible men attended therapists who provided pelvic floor muscle training (PFMT) and bladder training, while the control group continued with standard management.

In both intervention groups compliance with attending therapy and performing PFMT was high. However, this did not translate into differences in the chance of incontinence 12 months later. After radical prostatectomy, 76% still leaked urine in the intervention group compared with 77% in the control group receiving standard management, while after TURP, 65% were still wet compared with 62% in the control group. The interventions cost more, but there were no differences in any other clinical or economic outcomes.

We concluded that the provision of one-to-one conservative physical therapy for men with urinary incontinence after prostate surgery was unlikely to be effective or cost-effective compared with standard care (which includes the provision of information about conducting PFMT). We suggest that resources currently allocated to providing PFMT by a trained therapist in one-to-one consultations for men with incontinence after prostate surgery might potentially be better used elsewhere. The full results have recently been published in *The Lancet* and as a Health Technology Assessment monograph.

Previously the MAPS trial won the prize for Best Clinical Abstract at the International Continence Society Annual Meeting in Toronto, Canada in 2010. The prize (€1000) was donated to the prostate research charity Prostate Action by the MAPS team.

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John Norrie rejoins the Unit as Director of CHaRT

John Norrie rejoined the Unit as Director of the Centre for Healthcare Randomised Trials in September 2011. John had originally held the post from 2003 to 2008 and was highly instrumental in the successful registration of CHaRT by the UK Clinical Research Collaboration in 2007. Between 2008 and 2011 John held the post of Professor of Biostatistics and Clinical Trials at the Robertson Centre for Biostatistics in the University of Glasgow.

John is a highly experienced statistician and clinical trialist with over twenty years' experience in the field. His research interests involve the application of statistical methods to the design, conduct (e.g. sequential monitoring), analysis (e.g. risk modelling) and reporting of randomised controlled trials. John also sits on a number of prestigious grant funding panels such as the NIHR Health Technology Assessment Commissioning Board, the Marie Curie Cancer Care Funding Committee and the CSO ETMRC. John can be contacted on j.norrie@abdn.ac.uk or 01224 438179.

Comparative study of new imaging technologies for the diagnosis of glaucoma: the GATE study

Approximately 4000 people are registered either blind or partially sighted each year because of glaucoma in the UK. Many more people have glaucoma not severe enough to be registered, but severe enough to reduce vision and quality of life.



Glaucoma Automated Tests Evaluation

However, the diagnosis of glaucoma is challenging for health professionals and many people are incorrectly diagnosed as having glaucoma by community optometrists. In fact, only 20-30% of those referred from optometric services have glaucoma and 45% of patients are discharged after their first visit to the hospital eye department.

New automated diagnostic tests are available, which image the posterior part (fundus) of the eye, and are easy to perform. If one or more of the tests were proven to be sufficiently accurate (correctly detecting those with glaucoma and those without disease), patients without glaucoma would not need to be referred to an ophthalmologist, freeing up more time and resources to treat patients with eye diseases. People without glaucoma would not require lengthy examinations in the hospital eye department.

The National Institute for Health Research (NIHR) Health Technology Assessment (HTA) programme has funded the GATE

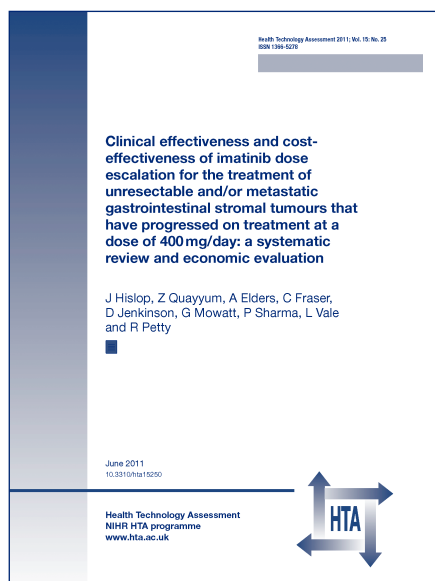
study which is led by Professor Augusto Azuara-Blanco. The study aims to compare the diagnostic performance of three automated imaging technologies within patients referred to secondary care with possible glaucoma and to explore patient test preferences.

A total of 954 people referred to four eye departments in the UK with possible glaucoma will be studied with three new diagnostic technologies; the Heidelberg Retina Tomograph (HRT-III), Scanning laser polarimetry (GDx-ECC) and Optical Coherence Tomography (Spectralis). The diagnostic test results will be compared against a reference standard of a comprehensive clinical examination by a consultant ophthalmologist. Participant preferences for the diagnostic tests will also be assessed.

The study will recruit patients from four UK centres, Aberdeen Royal Infirmary, St. Paul's Eye Unit, Liverpool, Hinchingsbrooke Hospital, Huntingdon, and Moorfields Eye Hospital in London. Recruitment to the study began in April 2011.

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The role of imatinib in gastrointestinal stromal tumours



Gastrointestinal stromal tumours (GISTs) are a rare cancer of the GI tract, affecting an estimated 900 people in the UK each year. Approximately 96% of cases have tyrosine kinase (KIT) - positive immunoreactivity. The National Institute for Health and Clinical Excellence (NICE) currently recommends treatment with imatinib at a dose of 400mg/day for KIT-positive patients with GIST for whom surgical removal of the

tumour(s) is not an option (i.e. patients with unresectable and/or metastatic forms of the disease). Dose escalation of imatinib, to a maximum of 800mg/day, is advocated by doctors for disease management. Recently NICE has also recommended sunitinib for patients who progress on imatinib treatment.

To clarify the relative effectiveness of these treatments, we reviewed the available evidence on dose-escalated imatinib, compared with sunitinib and/or best supportive care for this group of GIST patients upon progression at the 400mg/day dose.

A systematic review was undertaken to determine clinical effectiveness. Five studies were identified. Data were essentially observational; no study had been designed specifically to assess treatment upon progression at the 400mg/day dose. Results

suggested around one-third of patients may show response or stable disease with imatinib dose escalation to 600mg/day or 800mg/day. Median overall survival did not exceed two years for any treatment. Confidence intervals for the 800mg/day dose and sunitinib overlapped, suggesting no significant overall survival difference for these treatments.

A systematic review of cost-effectiveness studies was also undertaken. Seven studies which had conducted a full economic evaluation were included. However, only two compared all three treatments (dose-escalated imatinib, sunitinib and best supportive care) and neither study applied to an NHS context. The definitions used, patterns of resources and measures of effectiveness also varied between studies.

An economic model then compared alternative treatment strategies, based on seven clinically plausible pathways involving various combinations of the treatments under consideration. Cost-effectiveness results are suggested that either best supportive care only, imatinib 600mg/day only, or imatinib 600mg/day followed by 800mg/day followed by sunitinib, would be the most cost-effective care pathway, depending on society's maximum willingness to pay for additional QALYs.

These results are subject to a considerable amount of uncertainty owing to the lack of available data for parameter estimates. Further research on this group of patients is required. This evidence was not sufficiently conclusive for NICE to recommend imatinib dose escalation for patients who progress on the 400mg/day dose.

The review has been published as an Health Technology Assessment monograph.

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Peer support initiatives

In recent decades, many health services have introduced peer support interventions for people with various conditions, including cancer. Broadly speaking, they all seek to promote social and communicative exchanges between patients, but they do this in diverse ways and with a range of aims. Peer supporters might be encouraged to listen to problems, try to understand feelings, share experiences, discuss practical ways of dealing with physical effects of diseases or treatments, and provide practical help, for example with transportation. An extensive literature demonstrates that facilitated peer support interventions that enable people with cancer to talk with others with similar experiences can create a sense of empowerment and community and influence a range of outcomes including morale, psychosocial functioning and quality of life.

Studies of peer support initiatives in the context of cancer have tended to focus on the views of those who accept offers of peer support. However, accepters are in a minority and drop-out rates are high. Few studies have considered the views of those who do not participate, or those who subsequently drop out, resulting in limited understanding about why people do not use these services.

This project examined peer support among people living with a urological cancer. It involved twenty-six in-depth interviews that investigated peoples' experiences of needing and receiving information and support among those who had and who had not used a new urological cancer centre within Aberdeen Royal Infirmary and its various peer support opportunities.

Study participants reported varied needs for engagement with facilitated peer support. A minority reported avoiding speaking with other patients in order to protect their own or the other patients' emotional wellbeing. Non-engagement or attrition in peer support interventions was found to be related to individual 'patient' factors (e.g. existing social support networks; or sense of adjustment and acceptance) but also those relating to the intervention itself (e.g. perceptions about the composition of any peer support group or the characteristics of a prospective peer supporter; timing issues etc).

Services offering facilitated peer support should recognise people's variable and contingent needs for support and be sensitive to the reasons that can make it more or less helpful to different people.

Findings from this study are informing the design and delivery of the peer support service offered within the urological cancer centre. A paper based on findings has also recently been published in Patient Education and Counseling.

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UCAN – urological cancer centre within Aberdeen Royal Infirmary

CSO Fellowship awarded to Karen Forrest Keenan



A Postdoctoral Training Fellowship in Health Services and Health of the Public Research has been awarded to Karen Forrest Keenan. The fellowship will focus on how to share information with children and young people about genetic risk and develop evidence-based services for patients and practitioners in this area. The project has been developed by Karen and her supervisors Professor Lorna McKee and Dr Zosia Miedzybrodzka based on her PhD

work and practical experience of working with individuals and families affected by genetic conditions.

Karen's previous academic work has shown that children and young people growing up at risk of developing and passing on serious inherited conditions feel poorly served by existing health services. Furthermore, parents can perceive a lack of information and support from healthcare professionals about how to share information with their children about genetic conditions. In order to improve this the project will encompass four phases: 1) clinical observations of practitioners' interactions with parents and young people and follow up interviews with patients; 2) a survey of genetics professionals about their views of current guidance and experience in clinical practice; 3) an analysis of practitioners' case notes and 4) an exploration of how young people discuss their risk and predictive testing issues on social networking sites. The project will initially use two adult-onset inherited disorders which have different implications for parents and children as examples: Huntington's disease and Familial Hypercholesterolaemia. Both are timely as they present gaps in knowledge and there have been calls for more evidence to identify young people's information and support needs.

The project will allow Karen to engage with innovative methods of conducting research with children and young people as health care users as well as develop collaborations with new research and patient groups e.g. HealthTalk Online, the European Huntington's Disease Network and Heart-UK. Overall, it will contribute needed evidence about what professionals and families should tell children about genetic risk, and in the long term this will lead to an improvement in the lives of those who grow up at risk of serious inherited conditions.

Karen's fellowship will continue to October 2014. It is a joint position within the Health Services Research Unit and Medical Genetics Group.

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Staff News

We welcome Elaine Adam (Research Fellow), Daryll Archibald (Research Assistant), Miriam Brazzelli (Senior Research Fellow), Moira Cruickshank (Research Fellow - TAR), Joy Eldridge (Trial Manager), Rehab Ismail (PhD Student), Nicola McCleary (PhD Student), Lynn McKenzie (Secretary/PA), Heather Morgan (Research Fellow), Sajid Mohammed (Programmer), Natalie Paterson (Receptionist), Brian Power (MRC PhD Student) and Kieran Rothnie (Research Assistant) to the Unit.

Jen Burr, Emma Hodgson-Bunnnett, Cecilia Lee and Sean Wang have recently left the Unit and we wish them well.

Nitrites in Acute Myocardial Infarction

Cardiovascular diseases (CVD) are the main cause of death in the UK, accounting for almost 200,000 deaths per year. One of the manifestations of CVD is acute myocardial infarction (MI, or heart attack). There are estimated to be approximately 125,000 acute MIs in the UK per year. Whilst early reperfusion (restoring of blood flow to the heart) plays an important role in reducing the infarct size (area of dead tissue resulting from failure of blood supply), the reperfusion process itself causes injury. Effective therapy aimed at reducing this reperfusion injury has the potential to substantially reduce the risk of developing heart failure after an MI. There is evidence from animal models to suggest that an injection of sodium nitrite prior to reperfusion may reduce the reperfusion injury.

NIAMI is a multi-centre, double-blind, randomised trial, funded by the MRC, evaluating sodium nitrite injection versus placebo. The primary outcome is the difference in final infarct size between sodium nitrite and placebo groups measured using Magnetic Resonance Imaging (MRI) and corrected for area at risk.

Men aged 18 years or over and women aged 55 or over presenting within 12 hours of the onset of chest pain who have myocardial infarction with other trial-specific clinical symptoms

(ST segment elevation of more than 0.1mV, with occlusion of the culprit related artery - TIMI grade 0 or TIMI grade 1), and for whom the clinical decision has been

made to treat with primary percutaneous coronary intervention will be eligible. Patients are recruited and randomised to either sodium nitrite or placebo. Blood samples will be taken every six hours for up to 72 hours after the injection. An MRI scan will be conducted at between 10-14 days and 6 months after the MI.

The study is led by Professor Frenneaux, Regius Professor of Medicine, and co-ordinated by the Centre for Healthcare Randomised Trials (CHaRT). The study will recruit at three UK sites – Aberdeen Royal Infirmary, St George's Hospital in Tooting, and the Royal Sussex County Hospital in Brighton. Recruitment began in August 2011.

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Staff profile - Alison Avenell

Alison Avenell joined the Unit in 1998, as a Clinical Research Fellow. She was subsequently funded by the Chief Scientist Office (CSO) of the Scottish Government Health Directorates as a Clinical Research Fellow to undertake research in the MRC funded RECORD trial, which examined the effect of calcium and/or vitamin D supplementation in the secondary prevention of osteoporotic fractures. She also led the MAVIS trial which examined the effectiveness of vitamin and mineral supplementation in preventing infections in older people, and helped



lead the SIGNET trial of glutamine and selenium supplementation in critical illness. She was a CSO funded Career Scientist and is currently Clinical Senior Lecturer and Honorary Consultant in Clinical Biochemistry, undertaking systematic reviews and randomised controlled trials of treatments for adult obesity, and under-nutrition in clinical practice. She continues to research the effects of vitamin and calcium on fractures, cardiovascular disease and cancer, working with colleagues in New Zealand, Denmark and England.

Recent publications

- (1) Campbell MK, Entwistle VA, Cuthbertson BH, Skea Z, Sutherland A, McDonald A, Norrie JD, Carlson R, Bridgman S, KORAL Study Group. Developing a placebo-controlled trial in surgery: issues of design, acceptability and feasibility. *Trials [serial on the Internet]* 2011;12(50) URL: <http://www.trialsjournal.com/content/12/1/50>.
- (2) Charles K, McKee L, McCann S. A quest for patient-safe culture: contextual influences on patient safety performance. *Health Serv Res Policy* 2011;16(suppl.1):57-64.
- (3) Che Hamzah J, Burr JM, Ramsay CR, Azuara-Blanco A, Prior M. Choosing appropriate patient reported outcomes instrument for glaucoma research: a systematic review of vision instruments. *Qual Life Res* 2011;20(7):1141-58.
- (4) Eccles MP, Hrisos S, Francis J, Stamp E, Johnston M, Hawthorne G, Steen N, Grimshaw JM, Elovainio M, Presseau J, Hunter M. Instrument development, data collection, and characteristics of practices, staff, and measures in the Improving Quality of Care in Diabetes (iQuaD) study. *Implement Sci [serial on the Internet]* 2011;6:61. <http://www.implementationscience.com/content/6/1/61>.
- (5) Glaucoma Platform Study Group, Burr JM, Campbell MK, Campbell SE, Francis J, Hernandez RA, Greene A, Hopkins D, McCann SK. Developing the clinical components of a complex intervention for a glaucoma screening trial: a mixed methods study. *BMC Med Res Methodol [serial on the Internet]* 2011;11:54.
- (6) Hislop J, Quayyum Z, Elders A, Fraser C, Jenkinson DJ, Mowatt G, Sharma P, Vale L, Petty R. Clinical effectiveness and cost-effectiveness of imatinib dose escalation for the treatment of unresectable and/or metastatic gastrointestinal stromal tumours that have progressed on treatment at a dose of 400mg/day: a systematic review and economic evaluation. *Health Technol Assess* 2011;15:25.
- (7) Lois N, Burr JM, Norrie J, Vale L, Cook J, McDonald A, Tennent L, McPherson G. Internal limiting membrane peeling versus no peeling for idiopathic full thickness macular hole: A pragmatic randomised controlled trial. *Invest Ophthalmol Vis Sci* 2011;52(3):1586-92.
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- (9) McDonald A, Treweek S, Shakur H, Free C, Knight R, Speed C, Thomas R, Campbell M. Using a business model approach and marketing techniques for recruitment to clinical trials. *Trials [serial on the Internet]* 2011;12(74) URL: <http://www.trialsjournal.com/content/pdf/1745-6215-12-74.pdf>.
- (10) Mowatt G, N'Dow J, Vale L, Nabi G, Cook JA, Fraser C, Griffiths TRL, Aberdeen Technology Assessment Review Group. Photodynamic diagnosis of bladder cancer compared with white light cystoscopy: systematic review and meta-analysis. *Int J Technol Assess Health Care* 2011;27(1):3-10.
- (11) Prior M, Che Hamzah J, Francis J, Ramsay CR, Castillo M, Campbell SE, Azuara-Blanco A, Burr JM. Pre-validation methods for developing a patient reported outcome instrument. *BMC Med Res Methodol [serial on the Internet]* 2011;11:112. Available from: <http://www.biomedcentral.com/1471-2288/11/112>.
- (12) Treweek S, Ricketts I, Francis J, Eccles M, Bonetti D, MacLennan G, Sullivan F, Jones C, Weal M, Barnett K. Developing and evaluating interventions to reduce inappropriate prescribing by general practitioners of antibiotics for upper respiratory tract infections: a randomised controlled trial to compare paper-based and web-based modelling experiments. *Implement Sci [serial on the Internet]* 2011;6(16) <http://www.implementationscience.com/content/6/1/16>.



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